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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/990,405	11/21/2001	Alan L. Mueller	072827-1905	4028

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EXAMINER	
OSTRUP, CLINTON T	

ART UNIT	PAPER NUMBER
1614	12

DATE MAILED: 11/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/990,405	Applicant(s) MUELLER ET AL.	
	Examiner Clinton Ostrup	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *7-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 19-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-24* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-24 are pending in this office action. Claims 7-18 have been withdrawn from consideration as being drawn to a non-elected invention. Claims 5-6 and 21-24 are free of art.

Priority

Priority to PCT/US99/15857, filed July 12, 1999 and U.S. Provisional Application Number 60/092,546, filed July 13, 1998, has been acknowledged.

Response to Applicant's Arguments/Amendment

Applicant's arguments filed July 14, 2003, Paper No. 9, to the rejection of claims 1-6, 19, and 20 under 35 U.S.C. 103(a) have been fully considered and deemed persuasive. Therefore, the said rejection has been withdrawn.

Claim Objections

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

The second occurrence of claim 21, which is obviously misnumbered, has been renumbered claim 22.

Election/Restrictions

Applicants' elected specie is free of art. Thus, the search and examination has been broadened to encompass additional species. The species encompassed by the

structure of claim 5, and claims dependent therefrom, are also found to be free of art. Therefore, claims 5-6 and 21-24 are free of art. Thus, the search has been expanded to additional species encompassed by the structure of claim 3, 4, 19 and 20.

Claim Rejections - 35 USC § 112, First Paragraph

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following precedent is believed relevant to the instant case.

Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 1568 (Fed.Cir.1997), *cert. denied,* 523 U.S. 1089, 118 S.Ct. 1548 (1998), holds that an adequate written description requires a precise definition, such as by structure, formula, chemical name, or physical properties, "not a mere wish or plan for obtaining the claimed chemical invention." *Eli Lilly*, 119 F.3d at 1566. The Federal Circuit has adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement ("Guidelines"), 66 Fed.Reg. 1099 (Jan. 5, 2001), which state that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics," including, *inter alia,* "functional characteristics *when coupled with a known or disclosed correlation between function and structure....*" *Enzo Biochem, Inc. v. Gen-Probe Inc.,* 296 F.3d, 316, 1324-25 (Fed. Cir. 2002) (quoting Guidelines, 66 Fed.Reg. at 1106 (emphasis

added)). Moreover, although Eli Lilly and Enzo were decided within the factual context of DNA sequences, this does not preclude extending the reasoning of those cases to chemical structures in general. Univ. of Rochester v. G.D. Searle & Co., 249 F. Supp.2d 216, 225 (W.D.N.Y. 2003).

Applying the reasoning of the above-cited case law to the facts at hand, the instant specification fails to provide an adequate written description of compounds having a NMDA IC_{50} of about 50nm to about 1uM as measured by the NMDA assay and a serotonin reuptake IC_{50} of less than or equal to 100nm as measured in the serotonin reuptake inhibition assay. The specification describes only a limited number of suitable compounds, which are characterized by NMDA IC_{50} of about 50nm to about 1uM as measured by the NMDA assay and a serotonin reuptake IC_{50} of less than or equal to 100nm as measured in the serotonin reuptake inhibition assay. No other detailed, relevant identifying characteristics are specified which would adequately describe other useful compounds having the requisite NMDA IC_{50} of about 50nm to about 1uM as measured by the NMDA assay and a serotonin reuptake IC_{50} of less than or equal to 100nm as measured in the serotonin reuptake inhibition assay.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 and 19-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 3 recite the limitations "the NMDA assay" and "the serotonin reuptake inhibition assay", however, there is insufficient antecedent basis for these limitations in the claims.

Claims 3, 5, and 19 recite the limitation "the chemical structure", however there is insufficient antecedent basis for this limitation in the claims.

Claim 20 is vague and indefinite because it describes "each X" however, claim 19, from which claim 20 depends teaches "X^1" and "X^2", not simply "X". Moreover, claim 3, from which claim 19 depends, teaches "X". Therefore, it is unclear if applicant is claiming the "X" of claim 3 or the "X^1" and "X^2" of claim 19.

Any remaining claims are rejected as depending from a rejected base claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-4 and 19-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jones et al., Substituted 1,1-Diphenyl-3-aminopro-1-enes and 1,1-Diphenyl-3-aminopropanes as Potential Antidepressant Agents, Potential Antidepressants, Journal of Medicinal Chemistry, 1971, Vol.14, No.2, pages 161-164 and further in view of Nowak et al., Adaptation of Cortical NMDA Receptors by Chronic Treatment with Specific Serotonin Reuptake Inhibitors, European Journal of Pharmacology 342, January 26, 1998, pages 367-370.

Jones teaches compounds meeting the structure limitations of clams 3, 4, 19 and 20. See: pages 161-163, particularly, page 163, Table III, compound 56. The primary reference teaches the compound exhibits antidepressant activity via its ability to antagonize reserpine-induced hypothermia in mice (ED_{10} 10mg/kg) and by inhibition of serotonin uptake at 10μg/ml (97%).

Although the primary reference teaches the treatment of mice with compounds meeting the structure of instant claims 3-4 and 19-20, the reference lacks the specific NMDA IC50 as claimed instantly in claims 1-4 and 19-20.

Nowak et al is being supplied as a reference to demonstrate that when structurally dissimilar selective serotonin reuptake inhibitors are administered, NMDA receptors a qualitatively similar adaptive change is observed at NMDA receptors. Nowak et al teach that the chronic administration of structurally dissimilar antidepressant compounds, which are selective serotonin reuptake inhibitors, eliminated high affinity glycine-displaceable [3H]CGP-39653 binding to the mouse cortex,

indicating that selective serotonin reuptake inhibitors produce qualitatively similar adaptive changes at NMDA receptors.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of treating depression, as taught by Jones by selecting a compound that selectively inhibits the uptake of serotonin and produces similar adaptive changes in NMDA receptors because of the reasonable expectation of developing a method of treatment of depression with a compound that selectively inhibits serotonin uptake by 97%.

1-3 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Astra Lakemedel Aktiebolag, EP 0000322 (322) and further in view of Nowak et al., Adaptation of Cortical NMDA Receptors by Chronic Treatment with Specific Serotonin Reuptake Inhibitors, European Journal of Pharmacology 342, January 26, 1998, pages 367-370.

322 teaches compounds having anti-depressive activity meeting the structure of instant claims 3 and 19. See: page 30-31. The primary reference teaches these compounds as inhibiting the uptake of serotonin in both *in vitro* and *in vivo* experiments. See: pages 27-29.

Although the primary reference teaches compounds that meet those of instant claims 3 and 19, and said compounds inhibiting uptake of serotonin both *in vitro* and *in vivo*, the reference lacks the specific NMDA IC50 as claimed instantly in claims 1-3 and 19.

Nowak et al is being supplied as a reference to demonstrate that when structurally dissimilar selective serotonin reuptake inhibitors are administered, NMDA receptors a qualitatively similar adaptive change is observed at NMDA receptors. Nowak et al teach that the chronic administration of structurally dissimilar antidepressant compounds, which are selective serotonin reuptake inhibitors, eliminated high affinity glycine-displaceable [3H]CGP-39653 binding to the mouse cortex, indicating that selective serotonin reuptake inhibitors produce qualitatively similar adaptive changes at NMDA receptors.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of treating depression, as taught by 322 by selecting a compound that selectively inhibits the uptake of serotonin and produces similar adaptive changes in NMDA receptors because of the reasonable expectation of developing a method of treatment of depression with a compound that selectively inhibits serotonin uptake.

1-3 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Astra Lakemedel Aktiebolag, EP 0028682 (28682) and further in view of Nowak et al., Adaptation of Cortical NMDA Receptors by Chronic Treatment with Specific Serotonin Reuptake Inhibitors, European Journal of Pharmacology 342, January 26, 1998, pages 367-370.

28682 teaches compounds having anti-depressive activity meeting the structure of instant claims 3 and 19. See: page 30-31. The primary reference teaches these

compounds as inhibiting the uptake of serotonin in both *in vitro* and *in vivo* experiments. See: pages 27-29.

Although the primary reference teaches compounds that meet those of instant claims 3 and 19, and said compounds inhibiting uptake of serotonin *in vitro* and *in vivo*, the reference lacks the specific NMDA IC50 as claimed instantly in claims 1-3 and 19.

Nowak et al is being supplied as a reference to demonstrate that when structurally dissimilar selective serotonin reuptake inhibitors are administered, NMDA receptors a qualitatively similar adaptive change is observed at NMDA receptors. Nowak et al teach that the chronic administration of structurally dissimilar antidepressant compounds, which are selective serotonin reuptake inhibitors, eliminated high affinity glycine-displaceable [3H]CGP-39653 binding to the mouse cortex, indicating that selective serotonin reuptake inhibitors produce qualitatively similar adaptive changes at NMDA receptors.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of treating depression, as taught by 322 by selecting a compound that selectively inhibits the uptake of serotonin and produces similar adaptive changes in NMDA receptors because of the reasonable expectation of developing a method of treatment of depression with a compound that selectively inhibits serotonin uptake.

1-3 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carnmalm et al., UK 1602290 and further in view of Nowak et al., Adaptation of Cortical

NMDA Receptors by Chronic Treatment with Specific Serotonin Reuptake Inhibitors, European Journal of Pharmacology 342, January 26, 1998, pages 367-370.

Carnmalm et al., teach compounds which are used to treat depression and said compounds meet the specific compound structure of instant claims 3 and 19. See: page 16-17. The primary reference teaches these compounds as inhibiting the uptake of serotonin in both *in vitro* and *in vivo* experiments. See: page 15, lines 12-60.

Although the primary reference teaches compounds which meet those of instant claims 3 and 19, and said compounds inhibiting uptake of serotonin *in vitro* and *in vivo*, the reference lacks the specific NMDA IC50 as claimed instantly in claims 1-3 and 19.

Nowak et al is being supplied as a reference to demonstrate that when structurally dissimilar selective serotonin reuptake inhibitors are administered, NMDA receptors a qualitatively similar adaptive change is observed at NMDA receptors. Nowak et al teach that the chronic administration of structurally dissimilar antidepressant compounds, which are selective serotonin reuptake inhibitors, eliminated high affinity glycine-displaceable [3H]CGP-39653 binding to the mouse cortex, indicating that selective serotonin reuptake inhibitors produce qualitatively similar adaptive changes at NMDA receptors.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of treating depression, as taught by Carnmalm et al by selecting a compound that selectively inhibits the uptake of serotonin and produces similar adaptive changes in NMDA receptors because of the reasonable

expectation of developing a method of treatment of depression with a compound that selectively inhibits serotonin uptake.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Clinton Ostrup whose telephone number is (703) 308-3627. The examiner can normally be reached on 8:00am - 4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel can be reached on (703) 308-4725. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Clinton Ostrup
Examiner
Art Unit 1614

Frederick Krass
Primary Examiner
Art Unit 1614

November 6, 2003